



## RESEARCH ARTICLE

### OCULOMOTOR DYSFUNCTION IN MIGRAINE IS RECURRENT PAINFUL OCULOMOTOR NEUROPATHY

**<sup>1</sup>\*Dr. Sanjoy Chowdhury, M.S., DNB, D. O., <sup>2</sup>Dr. Hitesh Patel, <sup>2</sup>Dr. Pratik Bhosale and <sup>3</sup>Nilanjan Chowdhury**

<sup>1</sup>(Medical and Health Services), Head of Ophthalmology, Bokaro General Hospital, Steel Authority of India Limited

<sup>2</sup>DNB Resident, Bokaro General Hospital, Steel Authority of India Limited

<sup>3</sup>Final MBBS Sikkim Manipal Institute of Medical Sciences, India

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#### ABSTRACT

Migraine is a paroxysmal disorder with accompanying neurological phenomenon. Oculomotor dysfunction is one of them. A prospective study was done to investigate the prevalence and features of oculomotor dysfunction in migraineurs. A questionnaire based on "International headache society" criteria were distributed among the persons coming with chief complaints of headache. Among 2200 persons, 200 were migraineurs and were followed up over a period of two years. Detailed neurological, psychiatric and ocular examinations including MR- angiography were done. Ten out of 200 migraineurs had 3<sup>rd</sup> nerve involvement either pupillary or total ophthalmoplegic. MR-angiograph revealed no pathological lesion. Riboflavin had favorable response in 40% cases.

#### INTRODUCTION

One in ten persons around this world suffer from migraine, yet it is one of the most misunderstood, misdiagnosed and often inappropriately treated condition. The term "migraine" refers to various headache syndromes and to the neurological phenomenon that accompany them. (Stephen and Lipton, 1994) Ophthalmoplegic migraine was a well-recognized entity and was included in the classification of migraine, formulated by 'International headache society'. Ophthalmoplegic migraine is a rare condition usually beginning in infancy or childhood and characterized by paralysis of ocular cranial nerves in association with vascular headache (Troost, 1996). New classification of "Headache" has replaced the clinical entity of Ophthalmoplegic migraine by recurrent painful ophthalmoplegic neuropathy (HIS, 2013). Oculomotor nerve involvement is the commonest form of neural disturbance in migraine and can range from internal Ophthalmoplegia in the form of mydriasis to total recurrent third nerve paralysis (HIS, 2013). A deficit in mitochondrial energy metabolism has reported to have a role in pathogenesis of migraine and Riboflavin was used in high doses as prophylaxis in one study (Miller, 1977). In this prospective study, we examined all the cases of Ophthalmoplegic migraine also studied the role of riboflavin in Ophthalmoplegic migraine. The aim was to study the incidence of migraine in general and that of

Ophthalmoplegic migraine in particular in our "Steel Township". The role of riboflavin in the treatment of migraine was also evaluated.

#### MATERIALS AND METHODS

A standard questionnaire, based on existing International Headache Society's diagnostic criteria was distributed to the patients or their parents who presented to our outpatient department with headache over a period of two years. Diagnostic criteria used for migraine in this study are mentioned below:

- Sudden headaches separated by symptom free intervals.
- Hemicrania.
- Abdominal pain & nausea or vomiting associated
- Throbbing headache.
- Complete relief after a period of rest.
- An aura or "strange sensations" prior to or during headache, and
- A family history of migraine.

The participants were also polled on several 'paramigrainous' symptoms, such as motion sickness, visual whiteouts, seizures and sleep disturbances. These symptoms are not considered diagnostic of migraine but have been frequently reported in association with migraine. 2200 questionnaires were distributed during 1995-96 with a 95% completion rate. A total 218 patients were suffering from

**\*Corresponding author: Dr Sanjoy Chowdhury**

(Medical and Health Services), Head of Ophthalmology, Bokaro General Hospital, Steel Authority of India Limited

migraine, of which 18 cases were lost in follow up and rest 200 patients were followed up over a period of two years to find out the incidence of oculomotor dysfunction in the migraineurs. Each ophthalmoplegic patient was subjected to detailed history, clinical and neurological, ophthalmological examination which included visual fields, colour vision, ocular motility and fundus examination. Accommodation (near point of blur) was measured on RAF rule. Pupillary size and reaction to light and near, response to 2% pilocarpine and presence of any conjunctival blanching were also noted. Based on the clinical presentations; they were divided into two groups:

- Pupillary group: mydriasis only,
- Ophthalmoplegic group: total 3<sup>rd</sup> nerve palsy or other cranial nerve involvement.

Besides routine investigations, CT scan with plain and contrast enhanced were done in all the cases, seven patients had undergone MR-angiography. All the patients with oculomotor dysfunction were treated with riboflavin (100 mg) for a maximum period of two months. Age and sex matched migraineurs without any ocular involvement was taken as control. Clinical parameters evaluated were: frequency of attack, need for acute management, patient's opinion, and oculomotor functions.

**RESULTS**

Mean age of the target population was 28 years and that of migraineurs were 18 years while it was 17 years in case of ophthalmoplegics. Ten patients out of the 200 migraineurs had oculomotor dysfunctions of which 8 cases had recurrent uniocular mydriasis and was included in the pupillary group.



**Fig1.**First attack (1996) of total third nerve paralysis on left side in a 18 years old male migraineurs with full recovery, only to recur on the other side



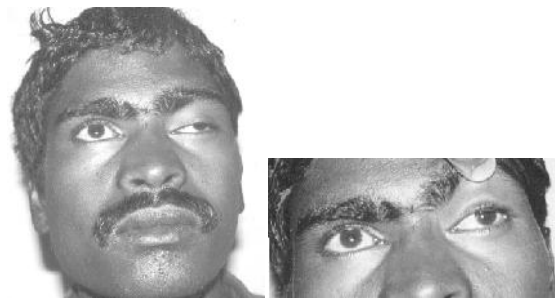
**Fig.2.**Complete ptosis with right divergent squint with total mydriasis fixing left and right eye alternatively

Two patients had alternating third nerve paralysis and were included in the Ophthalmoplegic group. 2 patients in the pupillary and both the cases of the Ophthalmoplegic group had shown favorable response to riboflavin. Reduced headache, reduced paramigrainous symptoms along with early recovery of oculomotor dysfunction were noticed with treatment. 4 cases of the controls had shown favorable response. The difference

was however not significant statistically ( $p > 0.05$ ). To summarize the results of this study, migraine was found in 10% of the target population though headache was the chief complaints in 30% of cases (n-610). 5% of the migraineurs had oculomotor dysfunction over two years period. Riboflavin was found effective in 40% cases. (Table. 1)

**Table 1. Results of riboflavin therapy**

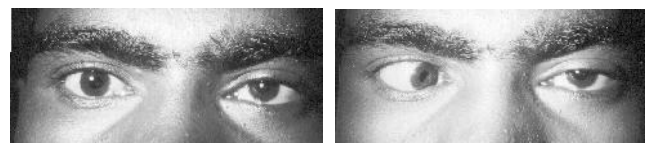
Category	Total	+Ve Response	Percentage
Pupillary group	8	2	25
Ophthalmoplegic group	2	2	100
Control (matching migraineurs)	10	4	40
Difference was not statistically significant ( $p > 0.05$ )			



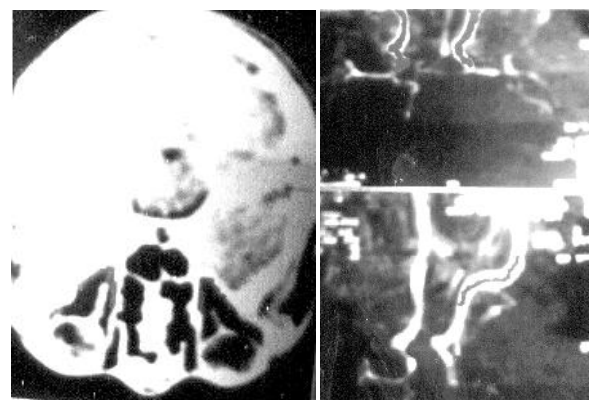
**Fig.3** After two years of symptom free interval, partial third nerve palsy recurred



**Fig.4.** Partial 6th nerve palsy on the left side in the same patient with complete recovery



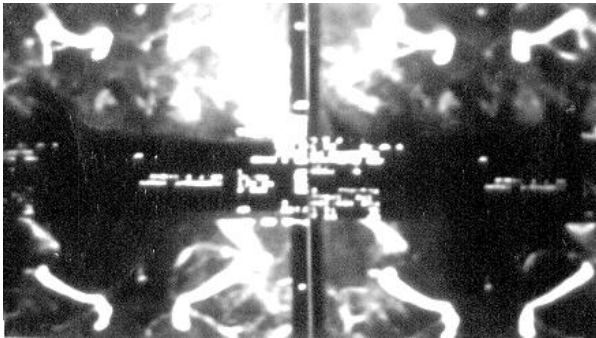
**Fig. 5.** Recurrence of 6th nerve palsy, now on rightside developed after 3months. Left eye fixing



**DISCUSSION**

Like Ophthalmoplegic migraine, recurrent painful ophthalmoplegic neuropathy is a rare condition usually beginning in infancy or childhood and characterized by

paralysis of ocular cranial nerves in association with vascular headache. The diagnosis of migraine is one of exclusion. Recurrent transient mydriasis without extra ocular involvement has not to my knowledge, been reported in any case of intracranial space occupying lesion.



**Fig.6. MRI and MR angiography showing normal pictures**

There is a 10% prevalence in the target population in our study among which 5% cases had oculomotor dysfunction. This was slightly less than other reports (Schoenen, 1998). Ophthalmoplegic migraine (or recurrent painful ophthalmoplegic neuropathy) is rare, with an overall incidence of 0.7 per million persons and affects less than 1% of migraines (Stang *et al.*, 1992). The diagnostic features of have been well described. It is a syndrome typically presenting in childhood characterized by recurrent unilateral headaches followed in hours or days by ophthalmoplegia. A family history of migraine is generally absent. Vasospasm with resultant ischemia of the oculomotor nerve is the presumed cause.

The oculomotor nerve is the most commonly affected cranial nerve in Ophthalmoplegic migraine, and Ophthalmoplegic migraine accounts for up to 7% of cases of isolated oculomotor nerve palsy in childhood. (Friedman *et al.*, 1962) The oculomotor nerve bifurcates into two divisions in the anterior cavernous sinus. The superior division innervates the levator palpebrae and superior rectus muscles, and the inferior division supplies the medial and inferior recti and inferior oblique muscles, as well as parasympathetic innervation to the pupil. None of the cases had any pathological lesion. This could be a manifestation of compressive (direct) or ischaemic (due to pressure on vasa nervorum) oculomotor neuropathy (2).

According to few researchers this could be due to (i) a pupillary sympathetic hypo function, and (ii) a cortical hypersensitivity to visual stimuli (perhaps only in migraine with aura), the pathogenesis of which remains to be determined. (Miller, 1977). This is a presumptive diagnosis and that other mechanisms including transient compression, edema, or ischemia of the appropriate portion of the oculomotor nerve may be involved. This rare presentation of presumed migraine or painful oculomotor neuropathy (as known now) manifest as isolated recurrent mydriasis or total third nerve palsy should be recognized to spare patients potentially harmful and expensive repetitive diagnostic testing. Migraine rarely responds to common analgesics. In this study, riboflavin was found effective in 40% cases, less than others (Schoenen *et al.*, 1994). Riboflavin increases mitochondrial energy by stimulating phosphorylation in the brain of the migraineurs. It appears from this study that migraine can cause episodic oculomotor dysfunction through different mechanisms. It also highlights that pupillary dilatation accompanied by headache is not always ominous and could be migrainous. Riboflavin could be a safe and cheaper alternative.

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